HMBS gene

hydroxymethylbilane synthase

Normal Function

The *HMBS* gene provides instructions for making an enzyme known as hydroxymethylbilane synthase. This enzyme is involved in the production of a molecule called heme. Heme is vital for all of the body's organs, although it is most abundant in the blood, bone marrow, and liver. Heme is an essential component of iron-containing proteins called hemoproteins, including hemoglobin (the protein that carries oxygen in the blood).

The production of heme is a multi-step process that requires eight different enzymes. Hydroxymethylbilane synthase is responsible for the third step in this process, which combines four molecules of porphobilinogen (the product of the second step) to form a compound called hydroxymethylbilane. In subsequent steps, five other enzymes produce and modify compounds that ultimately lead to heme.

Health Conditions Related to Genetic Changes

porphyria

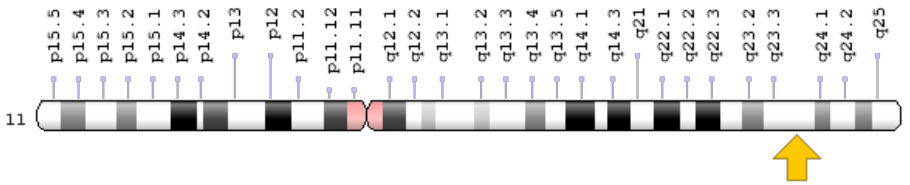
More than 300 mutations in the *HMBS* gene have been identified in people with a form of porphyria known as acute intermittent porphyria. Some of these mutations change single protein building blocks (amino acids) in hydroxymethylbilane synthase. Other mutations add or delete genetic material within the *HMBS* gene, which alters the structure and function of the enzyme.

Mutations in the *HMBS* gene reduce the activity of hydroxymethylbilane synthase, allowing compounds called porphyrins to build up in the liver and other organs. These compounds are formed during the normal process of heme production, but reduced activity of hydroxymethylbilane synthase allows them to accumulate to toxic levels. This buildup, in combination with nongenetic factors such as certain drugs, alcohol, smoking, and dieting, leads to attacks of severe abdominal pain and other symptoms in people with acute intermittent porphyria.

Chromosomal Location

Cytogenetic Location: 11q23.3, which is the long (q) arm of chromosome 11 at position 23.3

Molecular Location: base pairs 119,084,871 to 119,093,549 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- HEM3_HUMAN
- Hydroxymethylbilane Synthetase
- PBG-D
- PBGD
- Porphobilinogen Ammonia-Lyase
- Porphobilinogen ammonia-lyase (polymerizing)
- Porphobilinogen Deaminase
- Porphyrinogen Synthetase
- Pre-uroporphyrinogen synthase
- Preuroporphyrinogen Synthetase
- UPS
- Uroporphyrinogen synthase

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Mammalian Porphyrins Are Synthesized from Glycine and Succinyl Coenzyme A
  https://www.ncbi.nlm.nih.gov/books/NBK22446/#A3395

GeneReviews

- Acute Intermittent Porphyria
  https://www.ncbi.nlm.nih.gov/books/NBK1193

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28HMBS%5BTIAB%5D%29+OR+%28hydroxymethylbilane+synthase%5BTIAB%5D%29%29+OR+%28%28Hydroxymethylbilane+Synthetase%5BTIAB%5D%29+OR+%28Porphobilinogen+Ammonia-Lyase%5BTIAB%5D%29+OR+%28Porphobilinogen+Deaminase%5BTIAB%5D%29+OR+%28Porphyrinogen+Synthetase%5BTIAB%5D%29+OR+%28PBG-D%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- HYDROXYMETHYLBILANE SYNTHASE
  http://omim.org/entry/609806

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_HMBS.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HMBS%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4982
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3145
- UniProt
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